REMARKS

Reconsideration of the application is respectfully requested.

Claims 17, 22, and 23 have been canceled without prejudice or disclaimer.

Claims 1 and 24-26 have been amended to call for pharmaceutical combinations that provide greater than one dosage form. Support for these amendments is found throughout the specification, for example, at ¶¶13-17 of the published specification.

New claim 29 has been added. Support for the subject matter recited in new claim 29 is found in ¶17 of the published specification.

No new matter has been added. Upon entry of this amendment, claims 1-16, 18-21, and 24-29 are pending and at issue.

Rejections Under 35 U.S.C. § 101

Claims 22-26 have been rejected under 35 U.S.C. § 101 as reciting non-statutory subject matter. According to the Examiner, the claims embrace two different statutory categories of invention, viz., a product and a process, and thus it is unclear whether a product or a process is claimed. For the purposes of examination, the Examiner has treated these as product claims (*see* Office Action, pages 3-4).

Claims 22 and 23 have been canceled, thereby rendering this rejection moot as to these claims.

Claims 24-26 have been amended to call for a pharmaceutical combination that includes one or more unit dosage forms. This language makes it clear that the subject matter of these claims encompasses a product (and not a process). No new matter has been added by way of these amendments. Because the claims clearly embrace a product invention, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, first paragraph (written description)

Claims 1-28 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the specification fails to adequately describe a molar ratio or l-amphetamine to d-amphetamine released from the combination in a time period later in the day that is higher than the ratio released in a time period earlier in the day under any conditions (*see* Office Action, page 5). The Examiner also states:

- specific details and particular elements regarding the particular structure(s) that may be employed to achieve the claims release profile are not sufficiently described;
- although generic technologies are disclosed, a skilled artisan would have to conduct extensive experimentation using a variety of formulations to determine if the claimed release profile is achieved;
- the claims read upon any formulation used to result in the claimed release profile; and
- the specification is devoid of any description as to how the compositions operate to achieve the claimed release profile in such a manner that a skilled artisan would recognize that the compositions are capable of the claimed release profile.

Id. at pages 4-9.

Claims 17, 22, and 23 have been canceled, thereby rendering this rejection moot as to these claims.

As to the remaining claims, applicants traverse the rejection and respectfully request reconsideration.

The test for compliance with the written description requirement is whether the disclosure "*reasonably* conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 227 USPQ 177, 179 (Fed. Cir. 1985) (emphasis added).

Applicants have carefully considered the basis of the rejection, and submit that the premise of the Examiner's rejection is misplaced. The Examiner appears to take the position that since a specific combination ("recipe") of release compounds *that results in* the claimed release profile are not fully described, the claimed invention lacks adequate written description. However, the claimed invention calls for a composition that results in a specific *release profile* (ratio) of amphetamines during the day, rather than a particular sustained/delayed release combination ("recipe"). In other words, the claimed release profile during the day could be achieved by any number of sustained/delayed release formulations that a skilled artisan would be able to produce with knowledge that is well known in the art.

U.S. Patent No. 7,332,182 ("the '182 patent") is similar in this regard. Claim 1 of the '182 patent calls for an oral dosage form that includes an opioid analgesic, an opioid antagonist, and an irritant to impart an irritating sensation to an abuser upon administration of the dosage form after tampering. Claim 16 calls for the dosage form of claim 1 that has a ratio of opioid antagonist to opioid agonist that provides analgesia when administered orally, but that is aversive in dependent subjects when administered at the same or higher amount than the therapeutically effective amount. Here, the limitation of claim 16 is a ratio of opioid antagonist to agonist that results in variable effects, analgesia vs. aversion, depending on the amount taken. Claims 1 and 16 do not spell out particular opioid antagonists or agonists "structures" because the compounds (and ways of obtaining compounds with certain ratios) are well known in the art and are not limiting. Rather, it is the *ratio*, and *effect* of the ratio, depending on the amount taken that is limiting in the '182 patent. In the instant case, the limiting feature is that molar ratio of l-amphetamine to d-amphetamine released during the day. It is unnecessary to recite specific compositions that result in this release profile, just as the 182 patent does not specify particular compositions that result in variable opioid ratios depending on the amount taken.

In any event, the instant specification is replete with description of exemplary formulations ("recipes") that are capable of achieving the claimed release profile. For example, ¶¶33 and 36-52 of the published specification (U.S. Publication No. 2004/0220277) describe many such formulations, including for example, immediate, controlled, sustained, extended,

pulsatile etc., that can be used to achieve the claimed release profile. Example 6, for instance, describes how delayed release laminated beads and pulsatile delivery tablets could be used to arrive at the claimed invention, which is a particular release profile characterized in that the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day. The release profile could be achieved by a variety of combinations.

The Examiner appears to suggest that in order to adequately satisfy the written description requirement, disclosure that is currently "incorporated by reference" is *essential*, and therefore, the specification may need to be amended to recite this material (*see* Office Action, page 9, first complete paragraph). However, as stated above, none of the disclosed formulations are *essential* to obtain the claimed release profile, and the claimed release profile could be obtained using a variety of different formulations – all of which are conventional and well known in the art (*see, e.g.,* ¶ 33 of the published specification). It would be well within the knowledge of a skilled artisan which formulations to combine to arrive at an amphetamine combination having the claimed release profile. To incorporate all of the allegedly "essential" disclosure into the specification would require hundreds, if not thousands, of pages of disclosure. A patent need not teach, *and preferably omits*, what is well known in the art (*see,* MPEP § 2164.01) (emphasis added).

Finally, the proposed claim amendments call for a combination comprising separate unit dose forms. The claimed release profile could be achieved by a pharmaceutical combination that includes just d- or just l- amphetamine dosages given at the appropriate times during the day. The instant specification discloses a variety of ways that various release profiles can be obtained (*see, e.g.,* specification page 5). Further, individual unit dose forms and their administration were well known in the art at the time the application was filed, exemplified by art described by the Examiner in prior Office Actions.

In summary, the present claims call for a pharmaceutical combination that includes more than one unit dose form, *wherein the molar ratio of l-amphetamine to d-amphetamine*

released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day (or method of using such a combination). The claim feature represented in italics is a *release profile* that must be met to fall within the scope of the claims. A pharmaceutical combination that does not result in the recited release profile during the day would not infringe the claim, just as an opioid antagonist/agonist ratio that does not cause analgesia or aversiveness depending on the amounts taken would not infringe claims of the '182 patent. Therefore, this element of the instant claim language appropriately serves as a claim limitation. The release profile could be obtained by unit dose forms that are described in the specification, and about which detailed information is well known in the art (i.e., ways to make delayed release or immediate release unit dose forms that will create different release profiles).

Applicants submit that based on the foregoing, the specification at least *reasonably* conveys that the inventors had possession of the claimed invention. Thus, the written description requirement has been satisfied, and applicants respectfully request that this rejection be withdrawn, accordingly.

* * *

Claims 16-21 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. According to the Examiner, the specification fails to adequately describe limitations directed to "the time period later in the day being at least one hour following the period earlier in the day" (*see* Office Action, page 10). The Examiner notes that disclosure relevant to this claim limitation is found in ¶15 of the specification, but alleges that the disclose does not support the recited limitation.

Claim 17 has been canceled thereby rendering the rejection moot as to this claim.

As to claims 16 and 18-21, Applicants traverse the rejection and respectfully request reconsideration.

Applicants submit that the specification adequately supports the features called for in instant claim 16, i.e., an administration profile wherein relative amounts of the *d*- and *l*- isomers are administered at different times during the day with at least about one hour separating the "early" administration from the "late" administration.

First, the terms "early/earlier" and "late/later" are explicitly defined in the disclosure, and the disclosure states that: "there are least two periods in a day (e.g., typically each of a duration *of about one hour or more, e.g., about one to about four five, six, eight, etc.* hours) wherein the relative amounts of d- and l-amphetamines are different" (*see* published specification, ¶8) (emphasis added). A person of ordinary skill in the art, in fact an *ordinary* person, would instantly recognize that if there are at least two time periods in a day, one of them *must* be earlier and one of them *must* be later than the other. No other variation is possible. To emphasize this point, the specification states that with respect to the time periods, "the chronologically earlier occurring [period] is the early or earlier period and the chronologically subsequent period is the late or later period" (*id.*).

Second, numerous examples that constitute "early" and "late" periods are explicitly set forth, several of which are "at least about" an hour apart. For example, an earlier time period that is "before 10am" and a later time period that is "after 2pm" are at least about one hour apart, and would be recognized as such not only by skilled artisans, but also by ordinary people. Similarly, it would be understood that an early period occurring before noon would be at least about an hour before a late period occurring after 1pm, 2pm,or 6pm (*see* specification, ¶8). Therefore, not only are early and late periods defined with examples, but the examples enumerate several "variations" of early and late time periods, each example being at least an hour between the periods.

Finally, it is disclosed that "the relative amounts released of d- and l-amphetamines are different," and is typical (but not necessary) that "the ratio of l- to d-amphetamine released in the latest period will be higher than in all the other periods" (*id.*). The foregoing, therefore, provides ample disclosure that would indicate to those skilled in the art that Applicants were in

possession of the claimed feature of a time period later in the day being at least about one hour following the time period earlier in the day (*see, e.g., Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)). Therefore, this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 102 (b)

Claims 1-11, 14-15, and 22-25 remain rejected over U.S. Patent No. 6,322,819 ("Burnside"), and Patrick et al. for the same reasons set forth in the previous Office action. The Examiner has maintained the position that since *essential* structures are not recited, the claims are not limited by the recited release profile. The Examiner states that without calling for essential structures, "products of identical chemical composition can not have mutually exclusive properties" (*see* Office Action, pages 13-14).

Claims 22 and 23 have been canceled, thereby rendering this rejection moot as to these claims.

As to the remaining claims, applicants traverse the rejection and respectfully request reconsideration.

Applicants submit that the Examiner has improperly taken the position that certain structures resulting in the claimed release profile are "essential," and therefore must be recited in the claims. As set forth above, the claimed release profile could be obtained with any number of pharmaceutical compositions (e.g., various combinations of delayed and or pulsatile release beads, as set forth in the specification) that are well known in the art.

By analogy, no particular opioid antagonist/agonist combination is "essential" in the '182 patent claims to achieve a ratio that causes either analgesia or aversiveness depending on the amounts taken. In the instant case, the Examiner is requiring applicants to unduly narrow the claims by specifying a particular amphetamine "recipe" that result in the claimed release profile during the day. As noted, pharmaceuticals with variable release characteristics are well known in the art. and therefore need not be specified.

As to the Examiner's assertion that products with identical compositions cannot have mutually exclusive properties, this may be true for uniform compositions (*e.g.*, two batches of 1 cup water + 1 tablespoon sodium chloride will have the same properties). However, for example, two dose forms can have identical compositions by weight and matter, but vastly different release properties. For instance, consider one pill that has an acid-resistant shell and an acid-prone core, while a second pill has these same layers reversed (i.e., an acid-prone shell and an acid-resistant core). Even though these two hypothetical dose forms have the exact same composition by weight and matter, they would in fact have very disparate and mutually exclusive dissolution characteristics. Therefore, the blanket statement that products with identical compositions cannot have mutually exclusive properties is improper, and the argument is insufficient to support the broad proposition that pharmaceuticals with the same chemicals will necessarily have the same characteristics. The present claims set forth a particular property that the compositions *must* have, i.e., a composition wherein the molar ratio of l-amphetamine to d-amphetamine released from the pharmaceutical combination in a time period later in the day is higher than said ratio released therefrom in a time period earlier in the day.

For the foregoing reasons, the claimed amphetamine release profile is a limitation of the claimed composition, just as the ratio of opioids in the '182 patent claims discussed above is a limitation of that compound. The limiting release profile in the instant claims is not taught or suggested in the cited references. Accordingly, the references do not anticipate the present claims. Applicants respectfully request that this rejection be withdrawn, accordingly.

Rejections Under 35 U.S.C. § 103(a)

The Examiner has maintained the rejection of claims 1-28 as obvious over Patrick in view of WO 2002/039998, the '819 patent, STN Registry No. 156-34-3, and Tulloch et al., Pharmacotherapy, 2002;22(11):1405-1415. The Examiner has maintained the rejection asserting that the claim language calling for a molar ratio of l-amphetamine to d-amphetamine administered in a time period later in the day is higher than the ratio administered in a time

period earlier in the day, i.e. a specific release profile, fails to limit the claims because particular structural elements responsible for this feature are not recited.

Claims 17, 22, and 23 have been canceled, thereby rendering this rejection moot as to these claims.

As to the remaining claims, applicants traverse the rejection and respectfully request reconsideration.

For a claim to be obvious under U.S. patent law, the Examiner must explain why the difference(s) between the prior art and the claimed invention would have been obvious to one of ordinary skill in the art. Additionally, the Patent Office must articulate the reason(s) why a skilled artisan "would have recognized" that combining the prior art "would have yielded nothing more than predictable results" (*see* Examination Guidelines, Department of Commerce, *Federal Register*, 72(195):57529 (October 10, 2007).

Applicants reiterate that the molar ratio release profile called for in the claims is a claim limitation, and because many different compositions and dose administrations are well known in the art that could be used to arrive at the claimed release profile, these parameters are not "essential" and do not need to be recited in the claims. The cited references do not teach or suggest the presently claimed a release profile. Moreover, the references would not have led a reasonable person to predict that combining the prior art cited by the Examiner would have yielded "nothing more" than the claimed release profile, as required under the current patent guidelines. Therefore, the claims are also not obvious over the cited references. Applicants therefore respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining that the Examiner believes can be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

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